International Application No. PCT/GB93/02070, filed October 6, 1992, which is a continuation-in-part of U.S. Serial No. 07/958,248, filed October 8, 1992, now abandoned, the teachings of all of which are incorporated herein by reference.

In the Claims

Please cancel claims 1-31 without prejudice to applicants' right to pursue the subject matter of these claims in a continuing application.

Please add new claims 32-69 as follows:

32. (New) A method for treating or preventing a tumor necrosis factor-mediated disease in an individual in need thereof comprising co-administering methotrexate and a TNFα antagonist to said individual, in therapeutically effective amounts.

33. (New) The method of Claim 32, wherein said TNFα antagonist and methotrexate are administered simultaneously.

34. (New) The method of Claim 32, wherein said TNFα antagonist and methotrexate are administered sequentially.

35. (New) The method of Claim 32, wherein the tumor necrosis factor-mediated disease is selected from the group consisting of autoimmune disease, acute or chronic immune disease, inflammatory disease and neurodegenerative disease.

36. (New) The method of Claim 35, wherein said TNFα antagonist is administered in multiple doses.

37. (New) The method of Claim 32, wherein said TNFα antagonist prevents or inhibits TNFα synthesis or TNFα release.

38. (New) The method of Claim 37, wherein said TNFα antagonist is a phosphodiesterase inhibitor.

39. (New) The method of Claim 38, wherein said phosphodiesterase inhibitor is selected from the group consisting of pentoxifylline and rolipram.

40. (New) The method of Claim 37, wherein said TNFα antagonist is selected from the group consisting of thalidomide and tenidap.

41. (New) The method of Claim 38, wherein said TNFα antagonist is selected from the group consisting of an A2b adenosine receptor agonist and an A2b adenosine receptor enhancer.

42. (New) The method of Claim 36, wherein said TNFα antagonist is an anti-TNFα antibody or antigen-binding fragment thereof.

43. (New) The method of Claim 42, wherein said anti-TNFα antibody or antigen-binding fragment is a chimeric antibody or chimeric fragment, said chimeric antibody or chimeric fragment comprising a non-human variable region specific for TNFα or an antigen-binding portion thereof and a human

constant region.

44. (New) The method of Claim 43, wherein said chimeric antibody binds to one or more epitopes included in amino acid residues set forth in SEQ ID NO:1 or SEQ ID NO:2.

45. (New) The method of Claim 44, wherein said chimeric antibody competitively inhibits binding of TNFα to monoclonal antibody cA2.

46. (New) The method of Claim 44, wherein said chimeric antibody is monoclonal antibody cA2.

47. (New) The method of Claim 42, wherein said anti-TNFα antibody is a humanized antibody or antigen-binding fragment thereof.

48. (New) The method of Claim 47, wherein said humanized antibody binds to one or more epitopes included in amino acid residues set forth in SEQ ID NO:1 or SEQ ID NO:2.

49. (New) The method of Claim 42, wherein said anti-TNFα antibody is a resurfaced antibody or antigen-binding fragment thereof.

50. (New) The method of Claim 49, wherein said resurfaced antibody binds to one or more epitopes included in amino acid residues set forth in SEQ ID NO:1 or SEQ ID NO:2.

51. (New) The method of Claim 36, wherein said TNFα antagonist is a soluble TNFα receptor or functional portion thereof.

52. (New) The method of Claim 51, wherein said soluble TNFα receptor is selected from the group consisting of p55 TNFα receptor and p75 TNFα receptor.

53. (New) The method of Claim 51, wherein said soluble TNFα receptor is a TNFα receptor multimeric molecule.

54. (New) The method of Claim 51, wherein said soluble TNFα receptor is a TNFα receptor immunoreceptor fusion molecule

55. (New) A method for treating or preventing arthritis in an individual in need thereof comprising co-administering methotrexate and a TNFα antagonist to said individual, in therapeutically effective amounts.

56. (New) The method of Claim 55, wherein said TNFα antagonist and methotrexate are administered simultaneously.

57. (New) The method of Claim 55, wherein said TNFα antagonist and methotrexate are administered sequentially.

58. (New) The method of Claim 55, wherein said TNFα antagonist is administered in multiple doses.

59. (New) The method of Claim 55, wherein said TNFα antagonist prevents or inhibits TNFα synthesis or TNFα release.

60. (New) A method for treating or preventing rheumatoid arthritis in an individual in need thereof comprising co-administering methotrexate and a TNFα antagonist to said

individual, in therapeutically effective amounts.

61. (New) The method of Claim 60, wherein said TNFα antagonist and methotrexate are administered simultaneously.

62. (New) The method of Claim 60, wherein said TNFα antagonist and methotrexate are administered sequentially.

63. (New) The method of Claim 60, wherein said TNFα antagonist is administered in multiple doses.

64. (New) The method of Claim 60, wherein said TNFα antagonist prevents or inhibits TNFα synthesis or TNFα release.

65. (New) A method for treating or preventing Crohn's disease in an individual in need thereof comprising co-administering methotrexate and a TNFα antagonist to said individual, in therapeutically effective amounts.

66. (New) The method of Claim 65, wherein said TNFα antagonist and methotrexate are administered simultaneously.

67. (New) The method of Claim 65, wherein said TNFα antagonist and methotrexate are administered sequentially.

68. (New) The method of Claim 65, wherein said TNFα antagonist is administered in multiple doses.

69. (New) The method of Claim 65, wherein said TNFα antagonist prevents or inhibits TNFα synthesis or TNFα release.